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(WO/1990/012537) METHOD OF MEASURING THE FLOW WITHIN A BLOOD VESSEL AND DEVICE FOR PERFORMING THE METHOD

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Title: METHOD OF MEASURING THE FLOW WITHIN A BLOOD VESSEL AND DEVICE FOR PERFORMING THE METHOD

Abstract: The invention refers to a method and an apparatus which in situ measure the flow in a blood vessel mean (9). A local disturbance of the optical properties of the blood is performed at the measuring place. The disturbance is optically detected by means of an optical conduit (1) introduced into the vessel, the field of view of the conduit being directed towards the central portion of the vessel. The detected optical signal is used to form a measure of the flow. The device comprises a conduit introduced into the vessel up to the measuring place. A fibre optical light conductor (7) is provided within the conduit. According to the invention the end surface of the light conductor is bevelled to look into the central portion of the blood vessel. A light detector (7) is provided in the proximal end of the light conductor and detects the local disturbance of the optical properties of the blood. The disturbance may be brought about by introducing a fluorescent substance into the blood or by making use of the autofluorescence of the blood. Disturbances may also be brought about by locally producing microbubbles in the blood upstreams of the measuring position or by locally disturbing the orientation of the blood corpuscles.

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Method of measuring the flow within a blood vessel and device for performinη the method.

The present invention relates to a method of in situ measuring the flow within a blood vessel, e.g. a coronary heart vessel.

A known method for measuring blood flow makes use of an optical method based on Doppler-shift technique. A probe is applied to the skin and lightens a blood vessel. The light is reflected by blood corpuscles and, due to the movement of the blood corpuscles, undergoes a frequency shift, so called Doppler- shift. On the basis of the extent of the Doppler-shift it is thereafter theoretically possible to calculate the volume flow in the blood vessel illuminated by the probe.

A proposal has also been made to make use of the Doppler- shift technique for measuring the blood flow by inserting a light conductor into the vessel and illuminating the blood corpuscles. Reflected, frequency-shifted light is received by the light conductor and the Doppler-shift is measured. The extent of the Doppler-shift is an indirect measure of the flow in the vessel.

A disadvantage of the known technique resides in the fact that the circuits with which the Doppler-shifted signal is detected and filtered are complex and are unable to measure the Doppler-shift with a satisfactory exactitude. Another disadvantage of the Doppler-shift technique resides in the fact that the measuring result is dependent on the position within the cross-section of the blood vessel taken by the sensitive part of the light conductor when introduced into the vessel. It is well known that the speed profile of the flow in a tube is parabolic (when the flow is laminar). In order to be able to determine the flow it is thus necessary to know the position whithin the vessel taken by the optical light conductor, i.e. to know whether it is positioned centralⁿ ly of the vessel where the flow speed is at a maximum or towards the wall of the vessel where the speed may be practiⁿ cally zero. Normally, the light conductor will take a position in which it abuts against the wall of the vessel.

It is the purpose of the present invention to achieve a method and an apparatus which eliminate the above-mentioned disadvantages of the known technique and permit measuring in situ of the flow within a blood vessel independently of the position taken by the optical fibre within the blood vessel when inserted therein.

The method according to the invention is characterized in that a local disturbance of the optical properties of the blood is provoked at the measuring place, that the disturbance is optically detected by means of an optical conductor introⁿ duced into the vessel, the field of view of this conductor being directed towards the central portion of the vessel, and that the detected optical signal is utilized to produce a measure of the flow. The expression "field of view" refers to the spatial angle of the optical coupling of the light conducⁿ tor with the environment. Disturbances may be brought about by causing the light conductor to illuminate the blood with light of a first wave length for producing the natural fluoresⁿ cence of the blood. Alternatively the disturbance may be brought about by globally adding of a fluorescent substance to the blood to be illuminated from the light conductor with light in order to produce fluorescence, the fluorescent light being measured subsequently. A third alternative is to produce the disturbance of the optical properties of the blood by microbubbles of a gas being introduced locally into the blood at the measuring place and that the bubbles are illuminated with light from the light conductor. The amount of light reflected from the bubbles during their passage past the optical fibre is measured and forms a measure of the volume flow of the blood. According to a fourth method to produce the disturbance the orientation of the blood corpuscles is locally acted upon in order to produce a local turbulent flow which is illuminated with light from the light conductor. The amount of the light reflected by the blood corpuscles during their turbulent motion is measured when they flow past the field of view of the light conductor and forms a measure of the volume flow of the blood.

The invention also refers to a device for in situ measuring the flow of blood within a blood vessel. The device according to the invention is characterized in that the end surface of the light conductor is ground in order to cause its field of view to be directed inwardly towards the central portion of the blood vessel and that a light detector is provided in the proximal end of the light conductor to detect a local disturbance of the optical properties of the blood, and means for treating the detected light signal for obtaining a measure of the volume flow of the blood. According to a particularly preferred embodiment of the invention the distal end surface of the light conductor is obliquel ground.

The invention will be described in detail hereafter by reference to the attached drawings in which

Figure 1 schematically shows a device in accordance with the present invention.

Figure 2 is a detailed view of the measuring place in Figure 1,

Figure 3 is a detailed view of the end portion of a light conductor,

Figure 4 is a detailed view of an end portion of a modified light conductor,

Figure 5 shows a conduit into which the light conductor is inserted and through which gas is locally introduced at the measuring position for causing microbubbles to be formed,

Figure 6 is a side view of a non-pressurized conduit which in accordance with the present invention is used in order to bring about a local disturbance of the orientation of the blood corpuscles,

Figures 7 and 8 schematically show the orientation of the blood corpuscles prior and after the disturbance of the orientation of the blood corpuscles caused by the conduit according to Figure 6.

Figure 1 schematically shows the environment in which the invention is used. A conduit 1, the general construction of which is described in our international patent application PCT/SE87/00347, is introduced via the vena cava into the coronary artery of the heart to the measuring position shown in detail view in Figure 2. The light comes from a light source 2 which, for example, may be an arc lamp or a laser. The light from the light source passes through a filter 3 permitting light of a first wave length to pass. The filtered light is reflected by a semi-transparent mirror 4 and passes through a lens system 5 prior to entering into the proximal end of the conduit.

Figure 2 shows how the conduit in a way proposed by the present invention is provided with an opening 6 or a window releasing the light from a light conductor 7 introduced into the conduit against the proximal end surface of which the lens system 5 is focused. The field of view of the light conductor 7 is directed towards the central portion of the vessel as indicated by the broken lines 8 representing the field of view of the light conductor. The coronary vessel has the designation 9.

According to the invention there is provided a local disturbance of the optical properties of the blood. According to the invention four different measures are proposed for bringing about such a disturbance. These methods will be described in detail hereafter. The effect caused by the disturbance on the emitted light with which the blood is illuminated while flowing past the field of view 8 of the light conductor, is also detected by the end portion of the light conductor and this light spreads in the light conductor 7 rearwardly against

the incoming light and passes through the semi-transparent mirror 4, a second filter 10 to be detected by a photo-multiplyer 11 in which the light signal is reinforced and converted into an electric signal which thereafter is processed in electrical circuits, not shown, for obtaining a singnal representing a measure of the volume flow of the blood in the coronary artery of the heart.

Figure 3 schematically shows how the end surface of the optical fibre of the light conductor 7 is bevelled in order to direct - based on the total reflection or alternatively by steam-application of a reflective metal layer on the fibre end - the incoming light inward towards the centre of the blood vessel. The light conductor has side-viewing properties. Hereby the result is obtained that the measuring always is performed on blood flowing at the highest flow speeds independently of the

position of the end of the light conductor. In Figure 3 the field of view of the light conductor is indicated by broken lines 8 and the flow direction of the blood is indicated by the continuous arrow whereas the path of the central light ray is designated by the broken arrow.

Figure 4 shows another embodiment of the light conductor in which the optical fibre of the light conductor is ground plain so that the field of view of the light conductor extends in the downstream direction. Also here the field of view of the light conductor is defined by broken lines, the path of a central light ray by a broken arrow and the flow direction of the blood by a continuous arrow. The embodiment according to Figure 4 is not side-viewing to the same high degree as the embodiment according to Figure 3 but is satisfactory if the disturbances are produced with the conductor shown in Figures 6 and 7.

The local disturbance changing the optical properties of the blood can be of one of the follwing four types:

Marking the blood by adding to the blood a substance that can

be caused to fluoresce. A smaller amount of the blood of the patient is tapped and mixed with a fluorescent substance (=marking), whereafter the mixture is reintroduced into the blood circulation system of the patient. To the optical conductor light is transmitted having a wave length optically exciting the marked blood corpuscles. The filter 3 produces this light frequency. When the light meets a marked blood corpuscle, the blood corpuscle will fluoresce and emit light of a different wave length. This light is reflected in a backward direction towards the end of the optical conduit. The filter 10 transmits this wave length to the photomultiplyer 9. The signal from the photomultiplyer may be used to measure the time during which the marked blood corpuscle remains within the field of view 7 of the light conductor. Knowledge regarding the distance passed by the marked blood corpuscle during the said time permits the speed of the blood corpuscle to be calculated. The distance is defined, for example, by the width of the field of view. The volume flow can be calcu¬ lated provided the cross-sectional area of the vessel is known, this area being found, for example, by ultra sound examination or contrast X-ray examination.

A suitable fluorescent substance is fluoresceine-isothiocyanat, =FITC. Other suitable substances are aridine orange, acridine red, XRITC, DTAF, fluorescent benzimidasol derivatives H33258 and H33342. Figure 2 shows how a marked blood corpuscle enters into the field of view of the light conductor and is fluorescing there.

Obviously, the local disturbance in this case is produced by exciting or illuminating the marked blood corpuscles.

Another way of bringing about a local disturbance is based on a closely related phenomenon called auto-phosphorescence. All organic substances have a natural fluorescence and a natural phosphorescence if the substance in question is excited by light of suitable wave length. Natural fluorescence is rela¬ tively easily discovered at low temperature but is subject in

the present case to the disadvantage that the light phenomenon is extremely short (order of magnitude some nano seconds) . The autophosphoroscence, however, is relatively durable, up to some seconds. The autophosphorescence reduces when the temperature increases. The most normal working temperature for phosphorescence is 77^{O}K. However, there are some substances performing phosphorescence at room temperature (compare Lloyd J: B.F. 1979). Talanta 26, 180. In this case the autophospho- rescent substance is excited by briefly illuminating the light conductor whith light of a suitable wave length obtained by suitable choice of the filter 3. The fluorescent light is detected in the same way as in the preceding example.

It is also possible to integrate the photomultiplyer signal obtained when the disturbance is obtained by the globally added, locally excited fluorescent sustance. The integral of the signal also here will be a measure of the volume passing by and thereby also of the volume flow.

A third way of producing a local disturbance of the optical properties of the blood is illustrated in Figure 5 and com¬ prises causing a gas introduced into the proximal end of the conductor to be emitted through the fine opening 12 provided in the mantle 13 of the conduit. This causes a zone of micro¬ bubbles to be conducted by the blood past the field of view 7 of the light conductor to be gradually absorbed by the blood. The gas may, for example, be air, oxygene or another suitable gas. In this case the light bubbles are illuminated by light from the light source and the bubbles reflect the light back towards

the light conductor as if they were bright steel balls (total reflection). The reflected detected light is amplified in the photomultiplyer 9 and the signal is treated on the same way as in the integrating procedure described above in order to produce an electric signal related to the volume flow of the blood. In Figure 5 the conduit 6 is shown to have a soft, flexible spirally wound point 14 and the light conductor is surrounded by a spiral 15.

An arrangement explaining how the gas may be introduced into the conduit is described in our Swedish patent application 8801517-7 and comprises a cylinder sealingly surrounding the mantle of the conduit, the light conductor extending through this cylinder which in one of its end surfaces has a connec¬ tion to the conduit 1. In the wall surface of the cylinder a side tube is provided having a Luer-connection to which gas is attached.

Bubbles may also be provided in ways different from those shown. For example it is possible to perform local electrolysis of blood upstreams in relation to the measuring position.

A fourth way to bring about a local change of the optical properties of the blood is shown in Figure 6. In this case the outer surface of the conduit 6 is provided with a balloon 16 which via an opening 17 in the mantle of the conduit is connected to a duct 18 which during a short period is pres¬ surized by a gas with subsequent discharge of the pressure, causing the balloon 16 to produce a disturbance of the laminar flow of the blood corpuscles. In laminar blood flow the blood corpuscles are assumed to arrange themself according to the law of least resistance, i.e. laying in the direction of flow. If the laminar flow is disturbed in the way as described the orientation of the blood corpuscles will be changed. Figure 7 shows the orientation of the blood corpuscles prior to the disturbance and Figure 8 the orientation of the blood corpuscles after the disturbance.

The reflected light is detected and amplified in the photomul¬ tiplyer 11.

In all cases the flow measurements must be synchronized with heart frequency so that the measurement always is performed at the same time during the heart cycle.

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WO 1990012537 19901101 CLAIMS

1. A method of in situ measuring the flow within a blood vessel, e.g. a coronary heart vessel, characterized in that a local disturbance of the optical properties of the blood is performed at the measuring place, that the disturbance is optically detected by means of an optical conductor (7) introduced into the vessel, the field of view of this conductor being directed towards the central portion of the vessel, and that the detected optical signal is utilized to produce a measure of the flow.

2. The method as claimed in claim 1, characterized in that the local disturbance is brought about by causing the light conductor to illuminate the blood with light of a first wave lenght for the purpose of producing autophosphorescence of the blood and that the phosphorescent light having a different wave length is detected.

3. The method as claimed in claim 1, characterized in that into the blood a substance is introduced which can be caused to fluoresce, that the disturbance is brought about by causing the light conduit to illuminate the blood with light of a first wave length causing the said substance to fluoresce, and that the fluorescent light having a different wave length is detected.

4. The method as claimed in claim 3, characterized in that the fluorescent substance is globally supplied to the blood.

5. The method as claimed in claim 1, characterized in that the disturbance is produced by microbubbles of a gas introduced locally into the blood upstreams of the measuring place, that the bubbles are illuminated by light from the light conductor (7) and that the light reflected by the blood is detected.

6. The method as claimed in claim 5, characterized in that the bubbles are produced by local electrolysis of the blood.

7. The method as claimed in claim 1, characterized in that the disturbance is produced by locally acting upon the orienta¬ tion of the blood corpuscles for producing a locally turbulent zone, that the turbulent zone is illuminated with light from the light conductor and that the light reflected in the blood is detected.

8. The method as claimed in any of claims 1-7, characterized in that the detected reflected light is converted into an electric signal which is integrated for obtaining a signal related to the flow.

9. The method as claimed in any of claims 2-4, characterized in that the time during which the light is detected is measured to form a signal related to the flow in the vessel.

10. The method according to any of the preceding claims, characterized in that the measurement is synchronized with the heart frequency and that the measurement is always performed at substantially the same time during the heart cycle.

11. A device for measuring in situ the flow of blood in a blood vessel, e.g. the coronary artery of the heart, comprising a conduit (1) intended to be inserted into the vessel to the measuring position, a fibre optical light conductor (7) disposed within the conduit and extending up to the distal portion of the conduit and a light detector disposed in the proximal end of the light conductor, characterized in that the end surface of the light conductor is ground in order to cause its field of view to be directed inwardly towards the central portion of the blood vessel and to detect a local disturbance of the optical properties of the blood while the blood is flowing past the field of view of the light conductor, and means for treating the detected optical signal for obtain¬ ing a signal in relation to the flow of blood.

12. The device as claimed in claim 11, characterized in that

the distal end surface of the light conductor is bevelled to bring about a total reflection or that the bevelled surface has a light reflecting metal cover.

13. The device as claimed in claim 12, characterized in that an opening (6) is provided in the distal end of the conductor and that the bevelled end surface is positioned in said opening.

14. The device as claimed in claim 11, characterized in that a fine opening (12) is provided upstreams of the distal end of the conduit (1), said fine opening being intended to produce microbubbles.

15. The device as claimed in claim 11, characterized in that in the proximal portion of the light conductor a light source (2) is provided to propagate light through the light conductor, a filtering lens- and lens system (3, 4, 5, 10) for receiving detected light and a photomultiplyer (11) for converting the detected light into electrical signals.